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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,263	11/27/2001	Hayat Onyuksel	27611/36928	2010

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	5

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/995,263	Onyuksel
Examiner	**Art Unit**
Gollamudi Kishore	1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 22, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-30* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Nov 27, 2001* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The preliminary amendment dated 3-22-02 is acknowledged.

Claim Objections

1. Claim 25 is objected to under 37 CFR 1.75© as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim; in instant case it depends from claim 21 which is a multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim 25 has not been further treated on the merits.

Claims included in the prosecution are 1-24 and 26-30.

Claim Rejections - 35 USC § 112

2.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-24 and 26-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear whether VIP/glucagon/secretin family of peptides are the active agents which are effective in treating numerous disease states recited in claim 1. There should have been a comma between cerebral palsy and sleep disorder. It is unclear what applicants intend to convey by 'feeding disorder'.

It is unclear as to how one can form multivesicular liposomes by mixing the lipid components as recited in claim 3. Since these are method claims, the step leading to the formation of multivesicular liposomes and the conventional liposomes should be recited in claim 1.

The last two lines of claim 15 recite "forming multilamellar liposome products having an average diameter of less than about 1000 nm. Since it would appear that the liposomes have the recited sizes and not the final products, the examiner suggests the deletion of 'products'.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 15-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 and 4-6 of U.S. Patent No. 6,197,333. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons: claims in said patent are product by process claims and the process is the same as instant process; the sizes of less than 300 nm in the claims of said patent fall within 'less than 100 nm' in instant claims. Instant VIP in claim 24 falls within 'therapeutic agent' claimed in claim 4 of said patent.

6. Claims 15-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,348,214. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons: instant claims and claims in said patent are drawn to a process of preparation of liposomes using the same lipid components. The limitation 'echogenic' recited in instant claims therefore, is deemed to be included in the generic liposomes recited in the claims of said patent.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

8. Claims 1-3 and 5-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paul (5,770,570) in view of Martin (5,225,212).

Paul discloses liposomal compositions containing VIP. According to Paul, these compositions are to be used for the treatment of diseases such as ischaemia and mental conditions. VIP is either encapsulated within the liposome or bound on the liposome (note the abstract, col. 3, line 65 through col. 5, line 20, Examples and claims).

What is lacking in Paul is the binding of the phospholipid to PEG.

Martin discloses a method of preparation of liposomes by mixing the phospholipids which include a phospholipid which is bound to a water soluble polymer (note the abstract, col. 3, line 1 through col. 4, line 10; col. 10, line through col. 11, line 62 and claims). Martin does not specifically teach that the drug can be loaded after the formation of liposomes. Martin however, on columns 10 and 11 appear to imply that the drug can be loaded by

different methods. According to Martin, PEG extends the circulation time of the liposomes (note the abstract).

The inclusion of PEG taught by Martin in the liposomes of Paul for the preparation of liposomes containing VIP and use these liposomes for the treatment of disease states such as ischemia would have obvious to one of ordinary skill in the art since PEG extends the circulation time of the liposomes as taught by Martin.

9. Claims 1-3 and 5-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paul (5,770,570) in view of Martin (5,225,212), further in view of either of Caras (5,374,548), Noda (BBA, 1994) and Keder (J. Immunotherapy, 1994) by themselves or taken together.

The reference of Caras shows that the drug can be loaded on to the already formed liposomes (note example 4).

Similarly, Noda teaches incubation of already formed liposomes withe VIP to load VIP (note the abstract and page 325, col.1).

Keder discloses a process of preparation of liposomes and loading cytokines. The method involves the formation of liposomes and incubating the liposomes with IL-2 (note the abstract and page 49 and col. 1).

It would have been obvious to one of ordinary skill in the art to add a drug to the preformed liposomes of Martin with the expectation of obtaining similar results, since

Martin himself teaches that the liposomes can be made by any art known method and the references of Caras, Noda and Keder show that the liposome formulations and technique of such loading are art known.

10. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Paul in view of Martin (5, 225212) or Paul in view of Martin (5,225,212) in further view of Caras, Noda and Keder cited above, further in view of Kirby (Biotechnology, 1984 of record).

Martin's method does not involve dehydration and rehydration of the liposomes.

Kirby while disclosing a method of preparation of liposomes by dehydrating the lipid vesicles and then rehydrating them, teaches that such a method would result in a uniform sized liposomes and that the method is simple and can be used on an industrial scale (note pages 979 and 983).

The introduction of the dehydration-rehydration procedure in the method of preparation of liposomes of Martin would have been obvious to one of ordinary skill in the art because of the advantages of such a step taught by Kirby.

11. Claims 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paul in view of Martin (5, 225212) or Paul in view of Martin (5,225,212) in further view of Caras, Noda and Keder cited above, further in view of Lanza (5,612,057).

The primary references do not teach a diagnostic method using the liposomes. The use of liposomes as the diagnostic agents would have been obvious to one of ordinary skill

in the art, with the expectation of obtaining similar results, since the reference of Lanza shows the routine use of liposomes for diagnostic purposes.

All of the references except Paul are already of record.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.

Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

May 30, 2003